Fig. 1

(prior art)

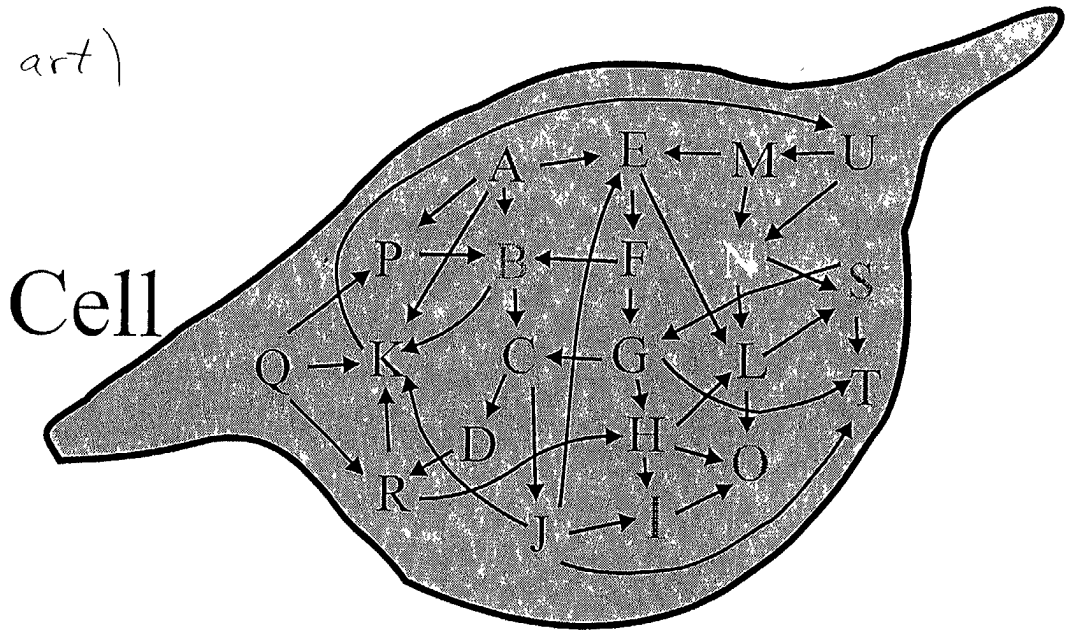


Fig. 2

(prior art)

MAP Kinase/Phosphoinositide/ PI3 Kinase Pathways in the Network

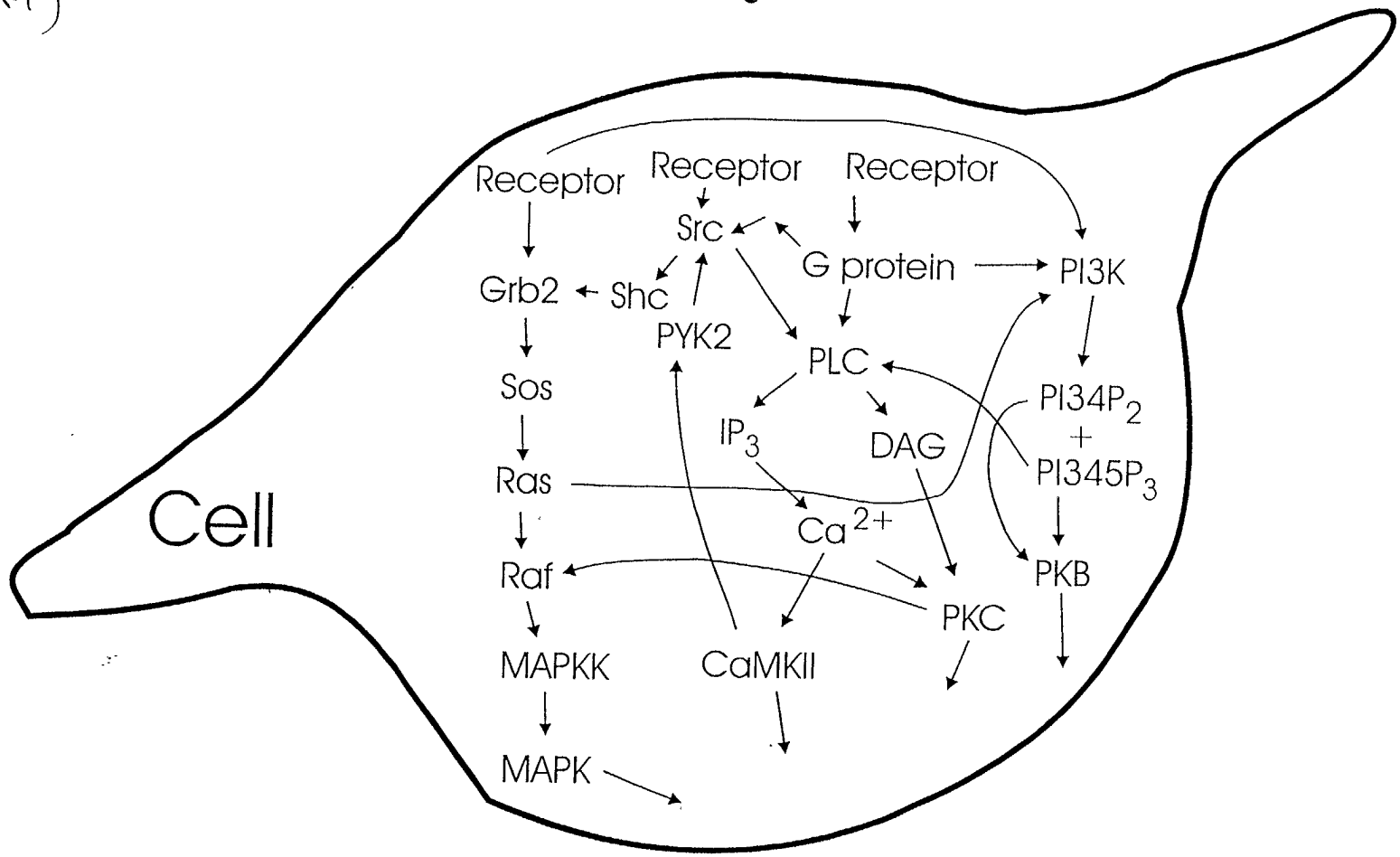
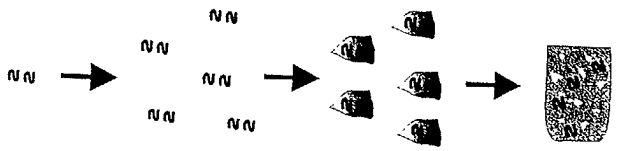


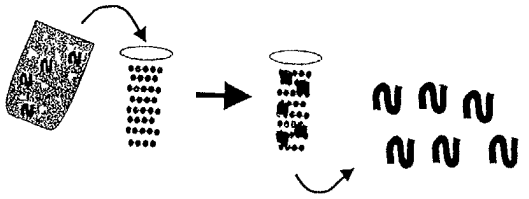
Fig. 3
(prior art)

Measurement of Kinase Activation (Current Technology)

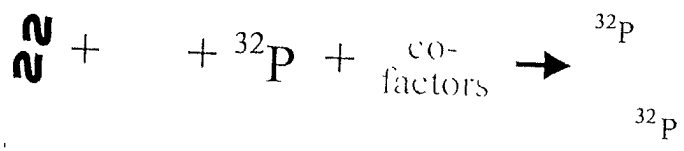
1. Grow up cells & prepare for assay (variable-days)



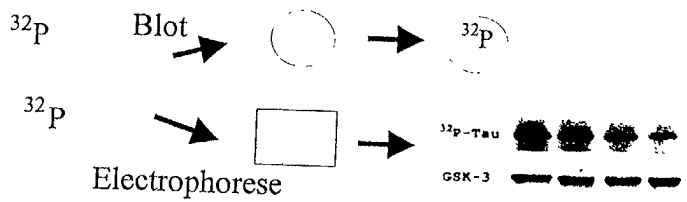
2. Immunoprecipitate the kinase (~4 hr)



3. Set-up and perform kinase reaction (hours)



4. Perform phosphocellulose assay or SDS-PAGE assay (hours-day)



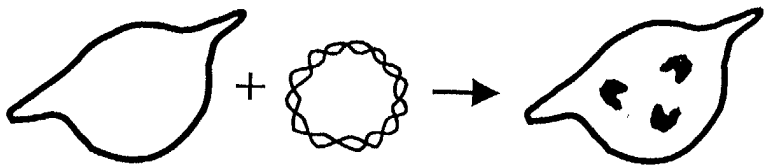
Assay Time ~Days

Fig. 4

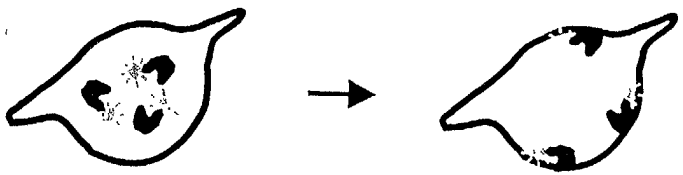
(prior art)

Measurement of Protein Location (via GFP Tag)

1. Develop stably transfected cell lines carrying the overexpressed GFP-tagged protein



2. Fluorescent imaging and pattern recognition

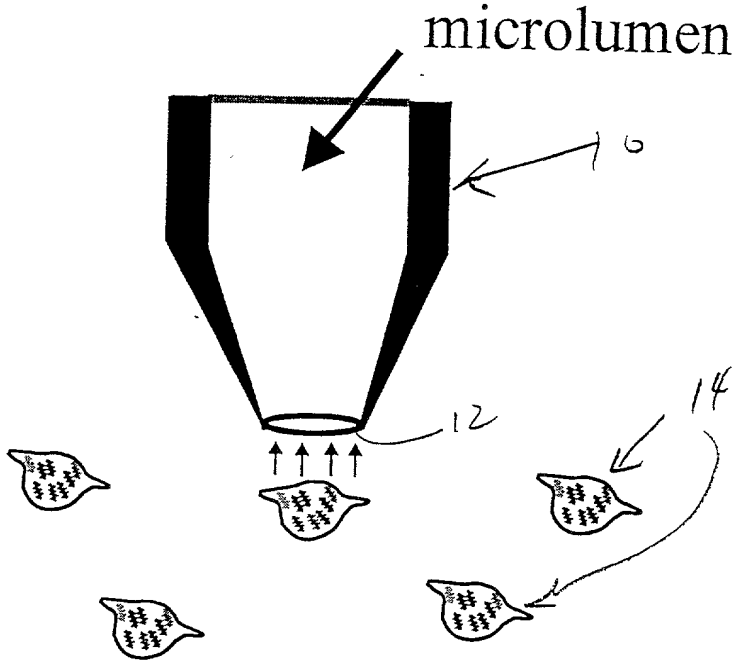


3. Infer protein activity from location

Assay Time ~Minutes

Fig. 5A

Single



Multiple

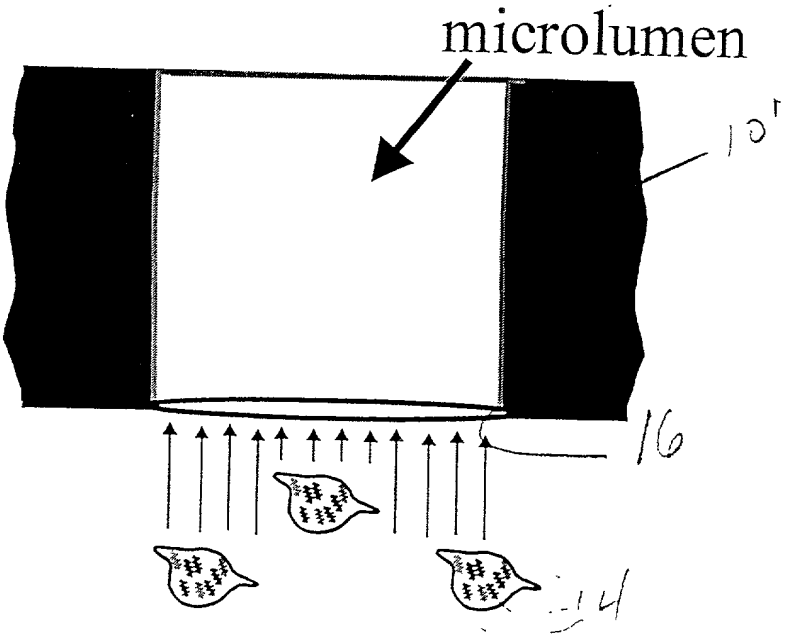
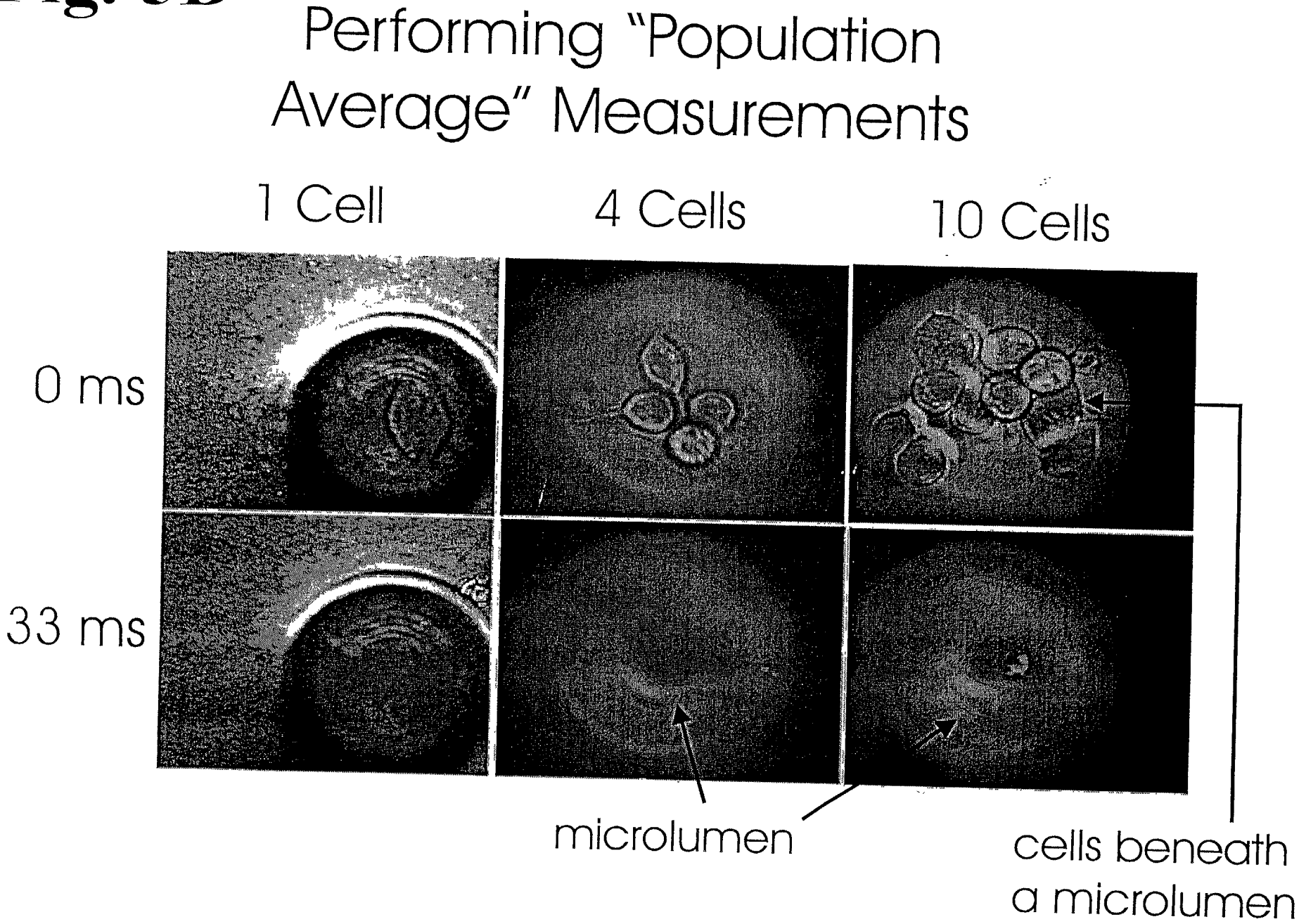


Fig. 5B


Performing "Population Average" Measurements
1 Cell
4 Cells
10 Cells
0 ms
33 ms
microlumen
cells beneath a microlumen

Single Cells or Population Averages

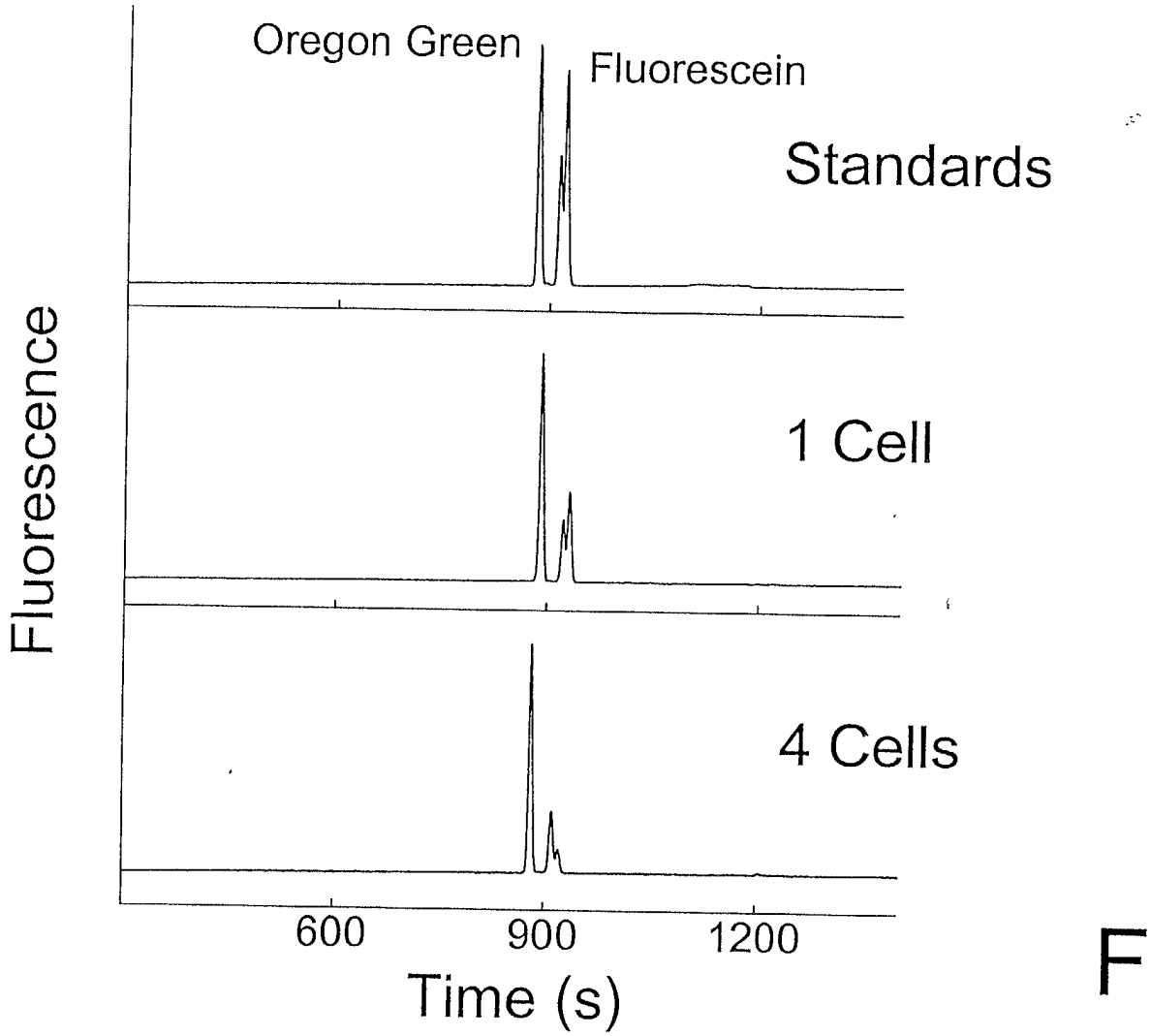


Fig. 5C

Fig. 6A Sampling a Portion of a Cell

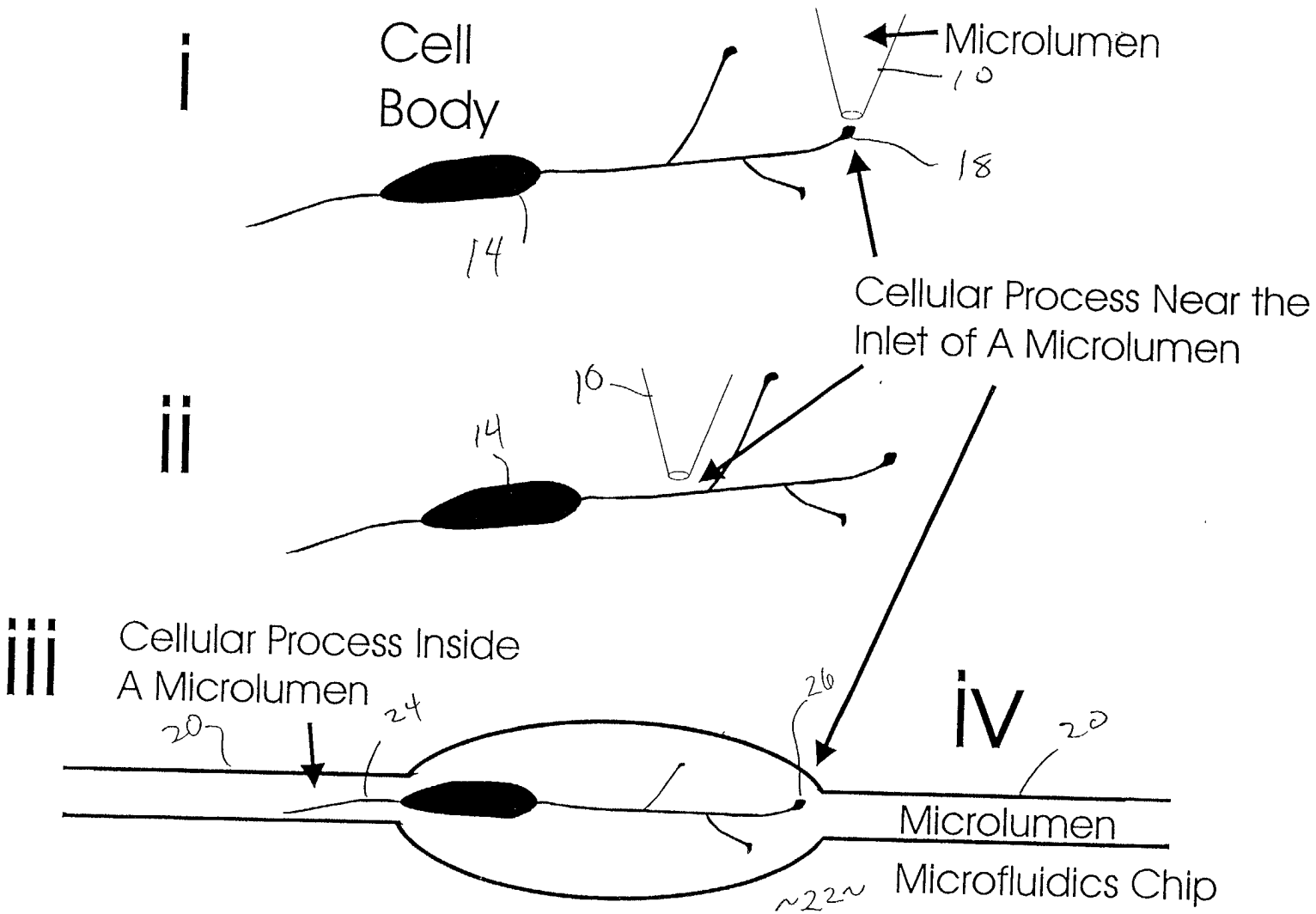


Fig. 6B

Sampling the Contents of a Neuronal Process

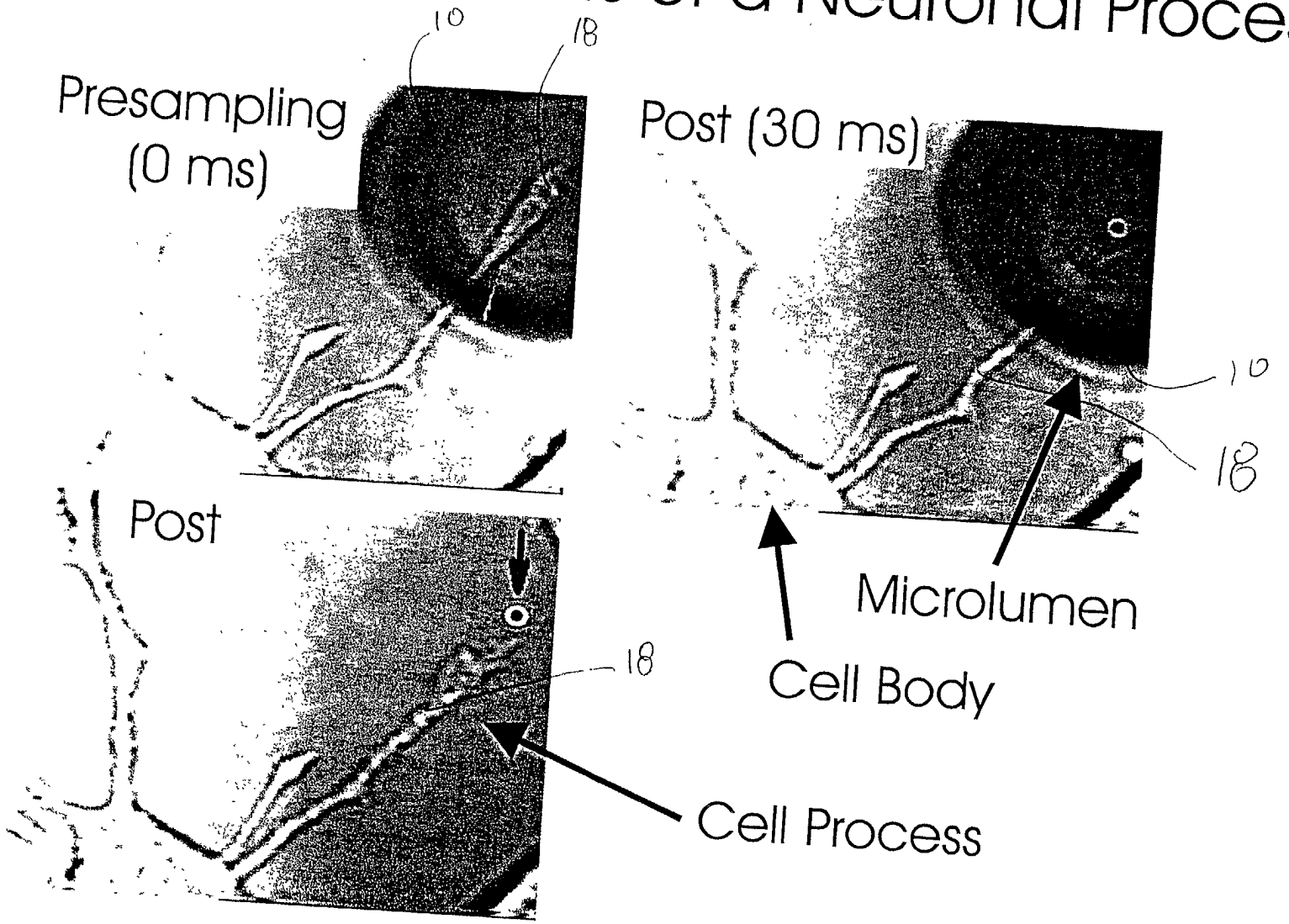


Fig. 6C

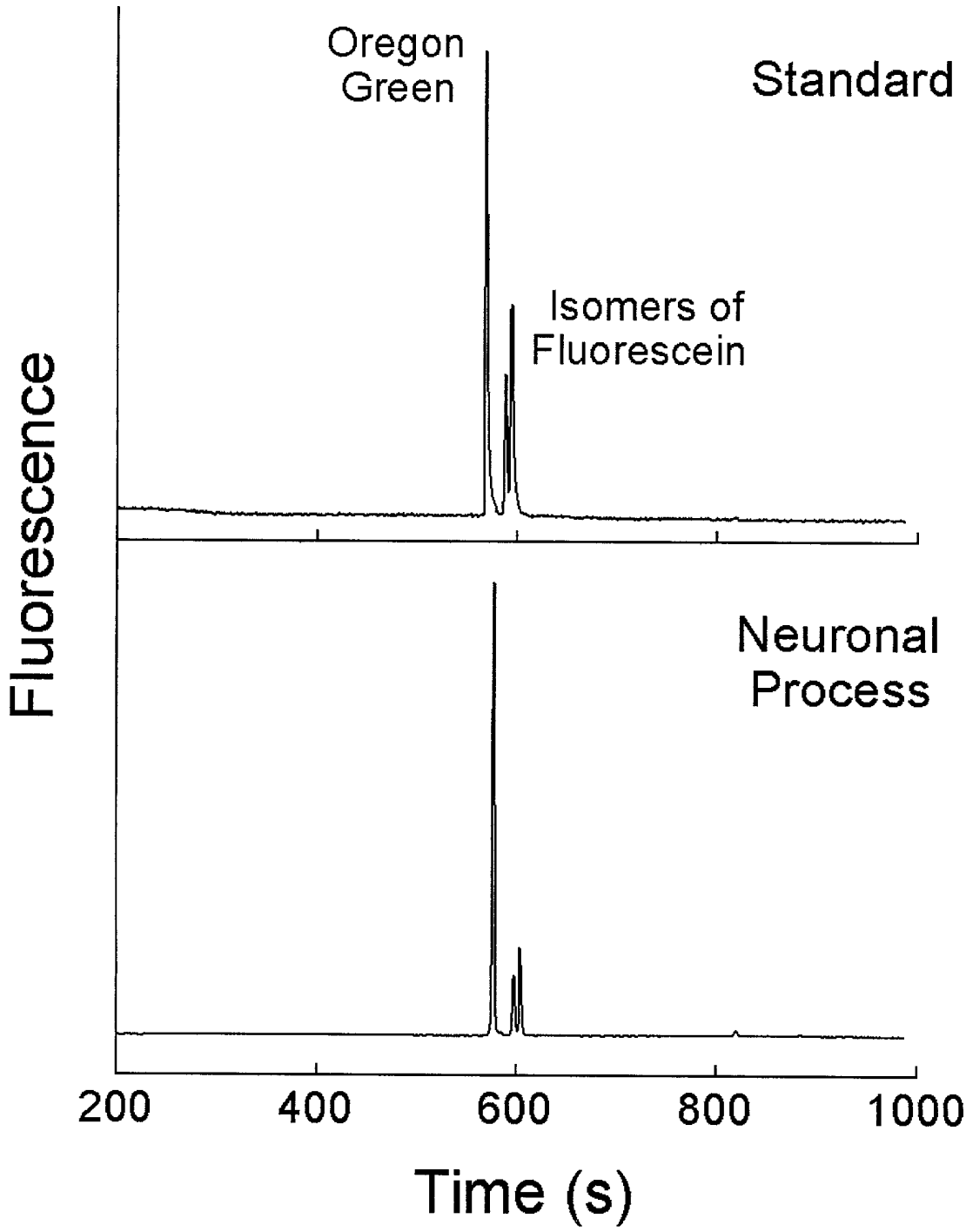

Analyzing A Neuronal Process
Oregon Green
Standard
Isomers of Fluorescein
Fluorescence
Neuronal Process
200
400
600
800
1000
Time (s)

Fig.7a Cell Assay

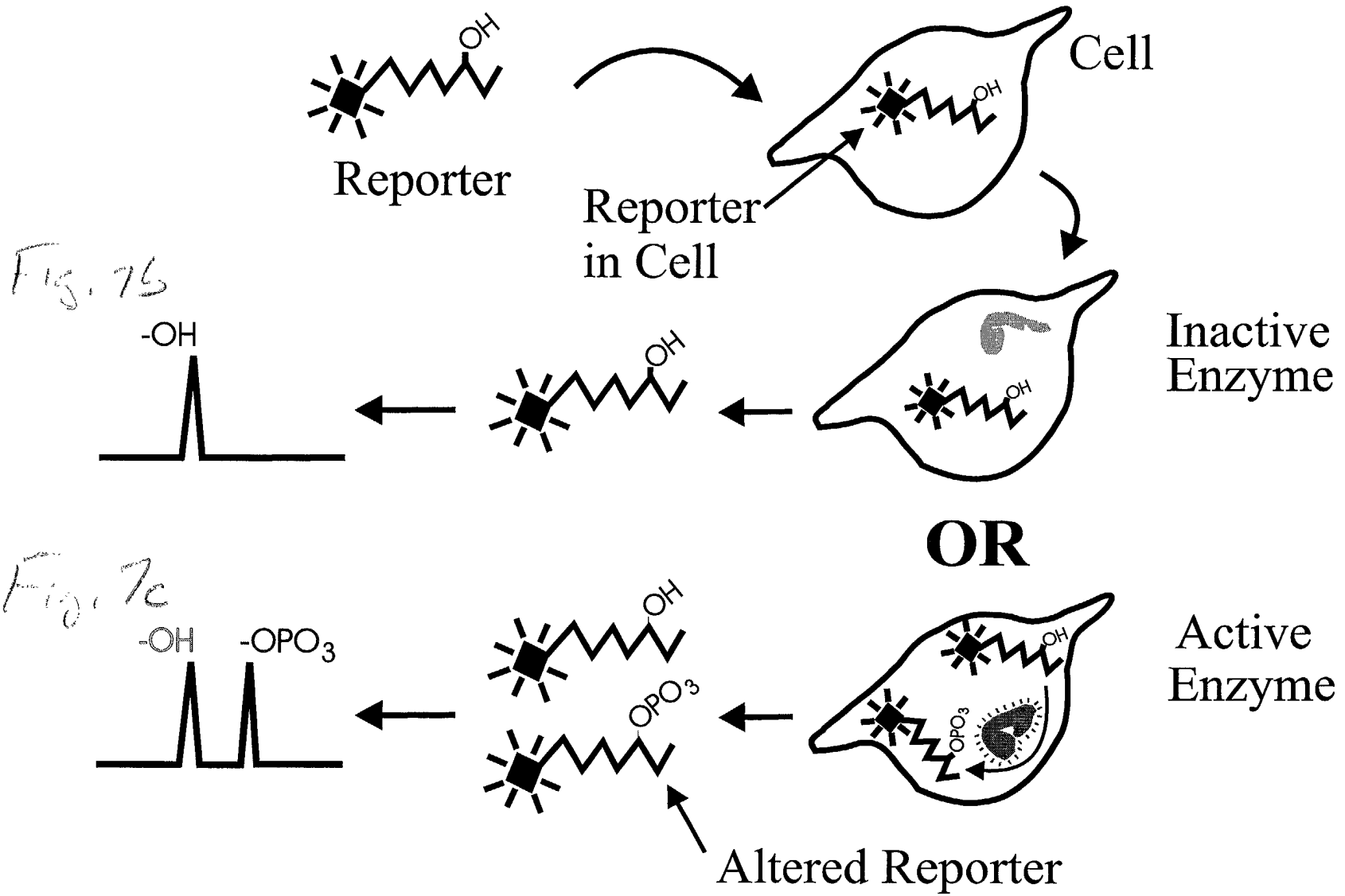


Fig. 8

Loading Single Cells With Enzyme Substrates

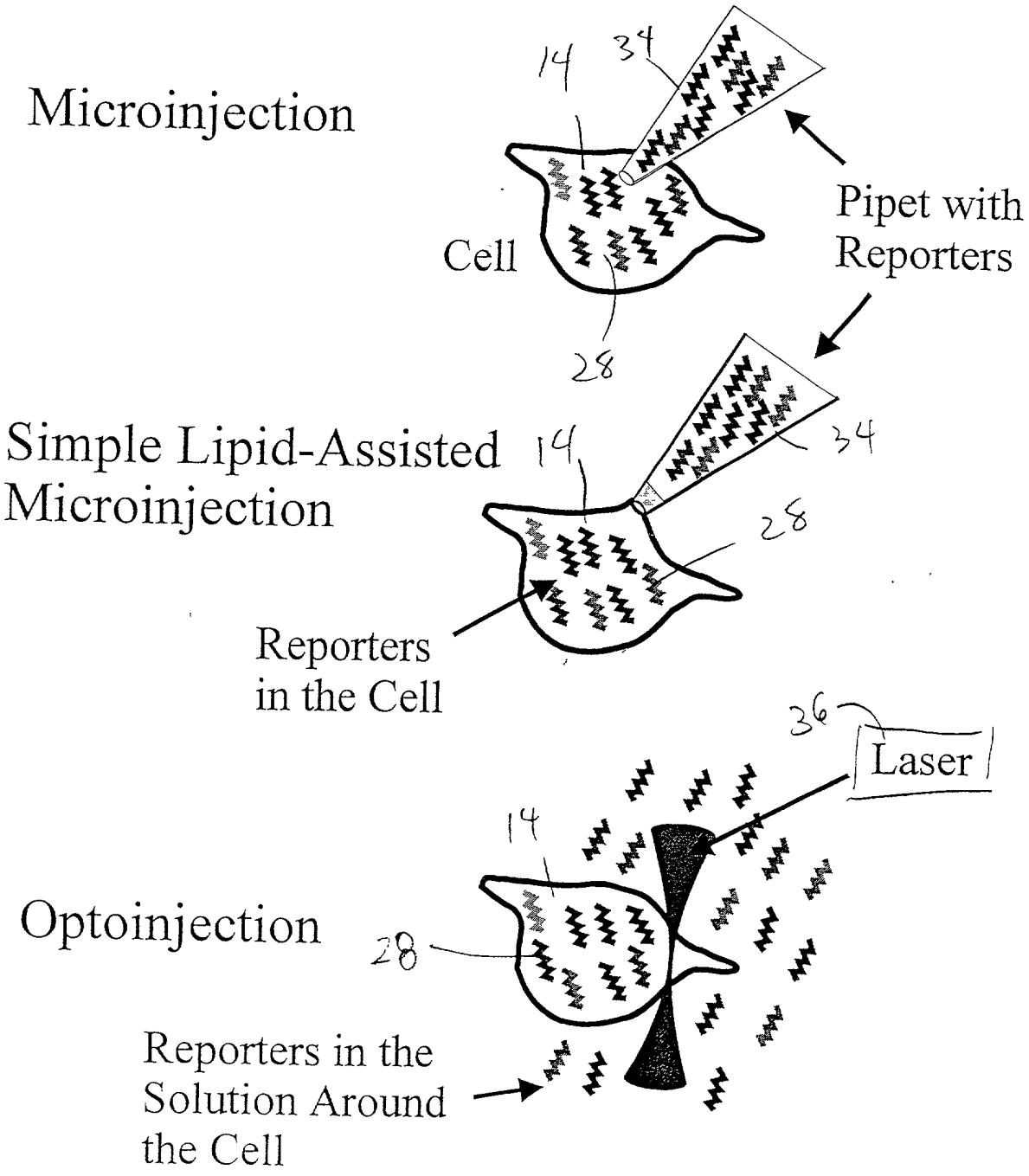
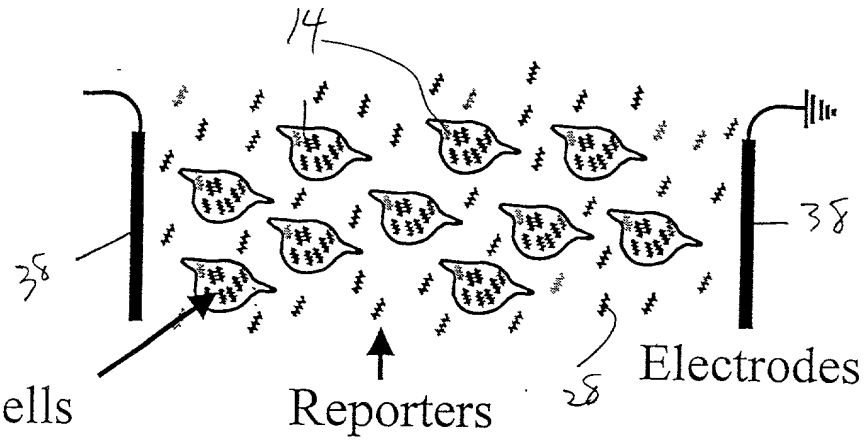


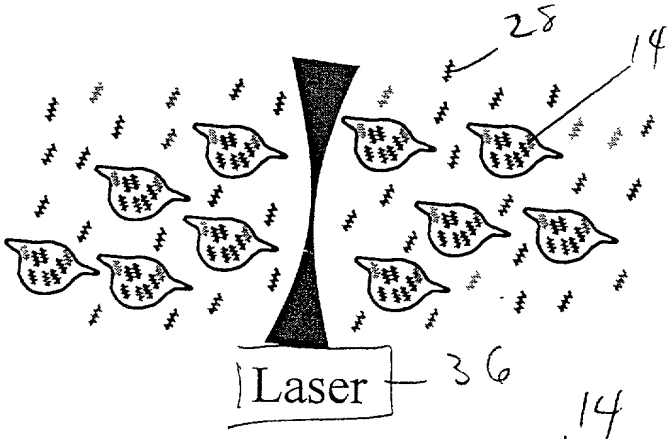
Fig. 9

Loading Multiple Cells With Enzyme Substrates

Electroporation



Optoporation



Passive Techniques

- Pinocytosis
- Vesicle Fusion
- Membrane-Permeant Substrates

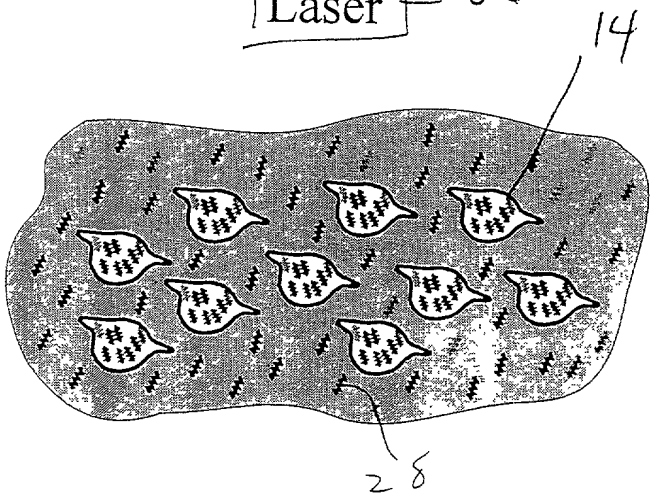


Fig. 10

Nuclear-Localized Substrate for PKC

Fluorescence Image Transmitted Light Image

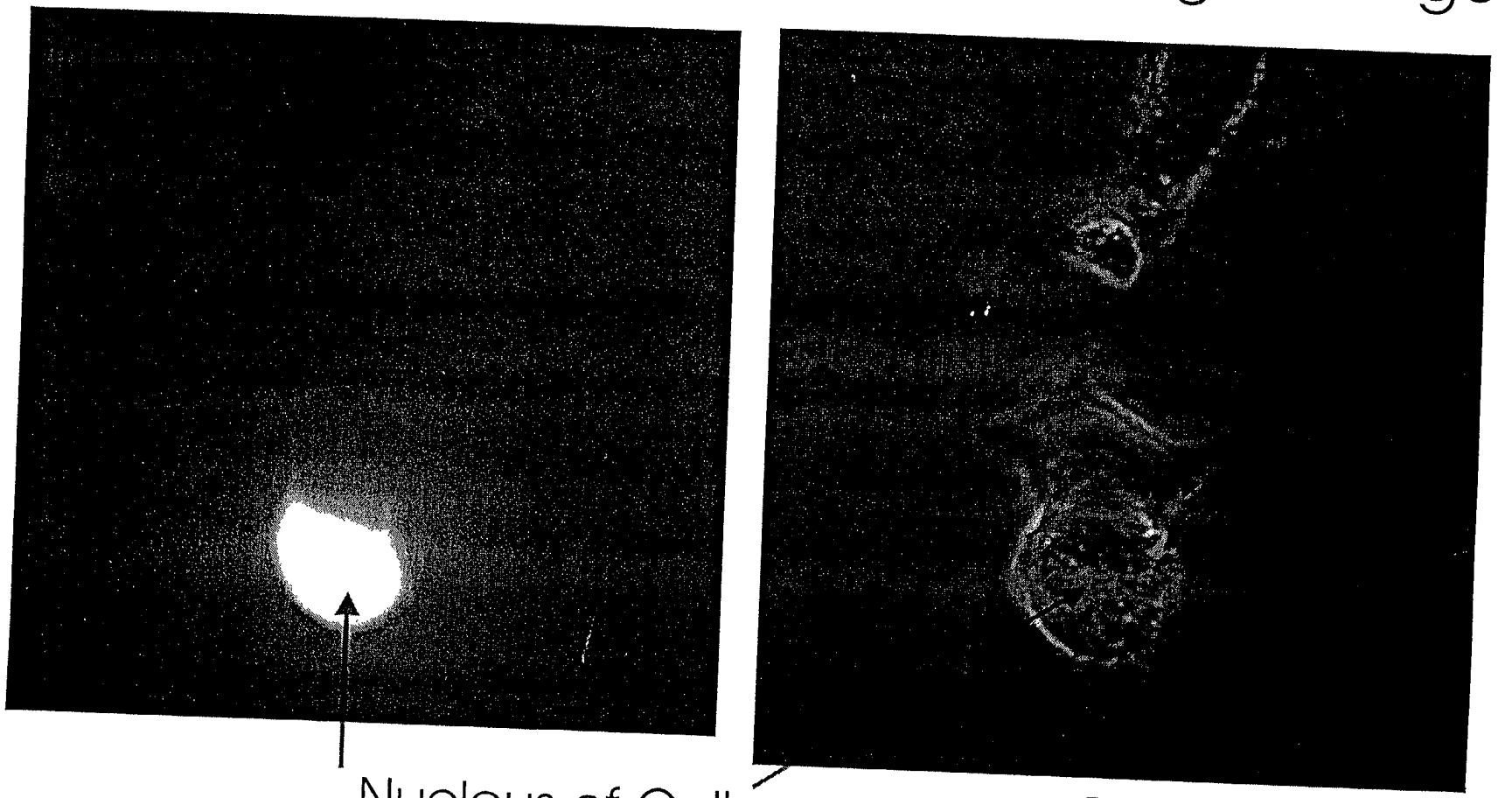


Fig. 11

Coupling to Other Technologies

Proteomics

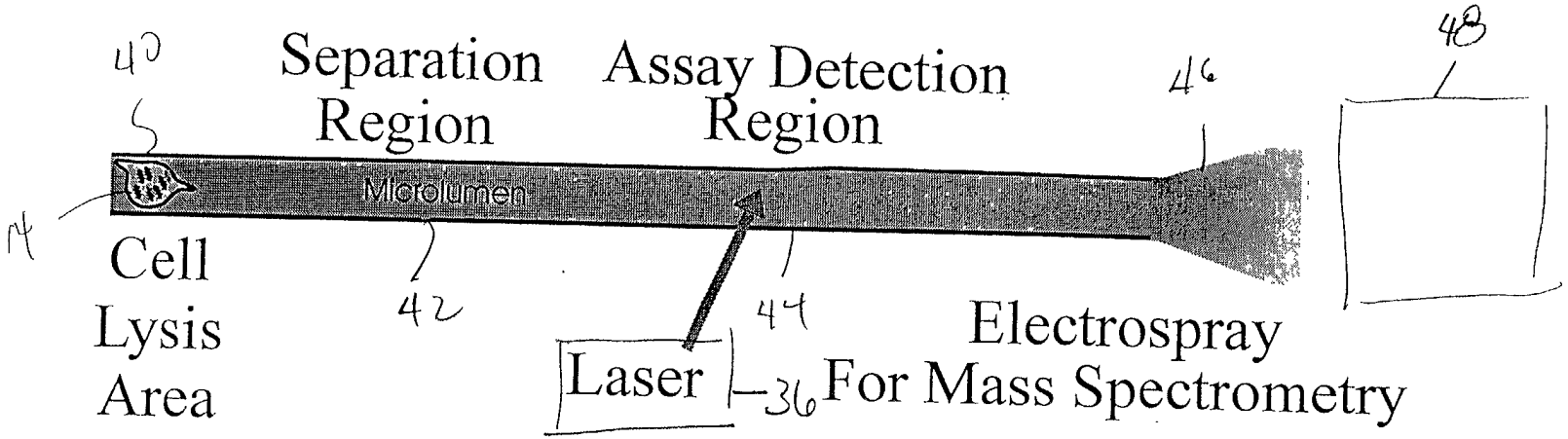


Fig. 12A

Coupling to Other Technologies

Genomics

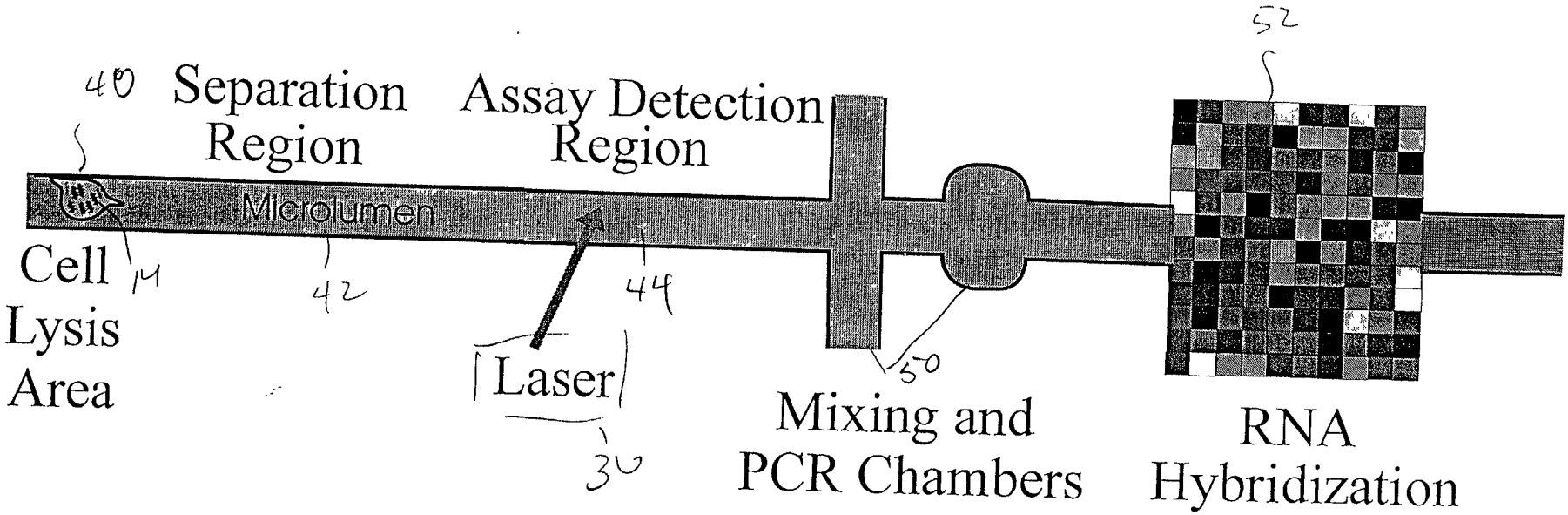


Fig. 12B

SIGNAL TRANSDUCTION MICROCHIP

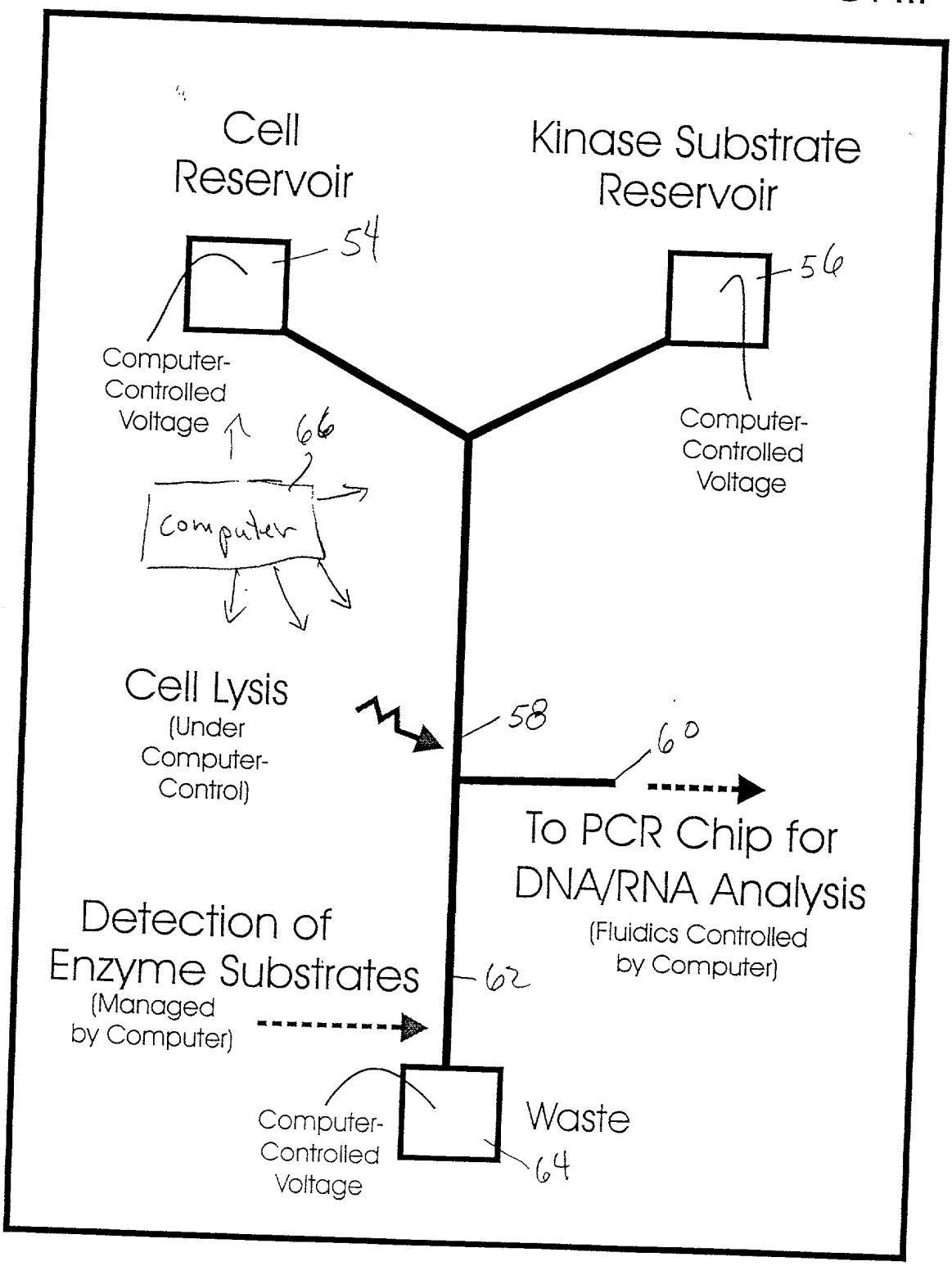


Fig. 13

Coupling to Other Technologies

Flow Cytometry

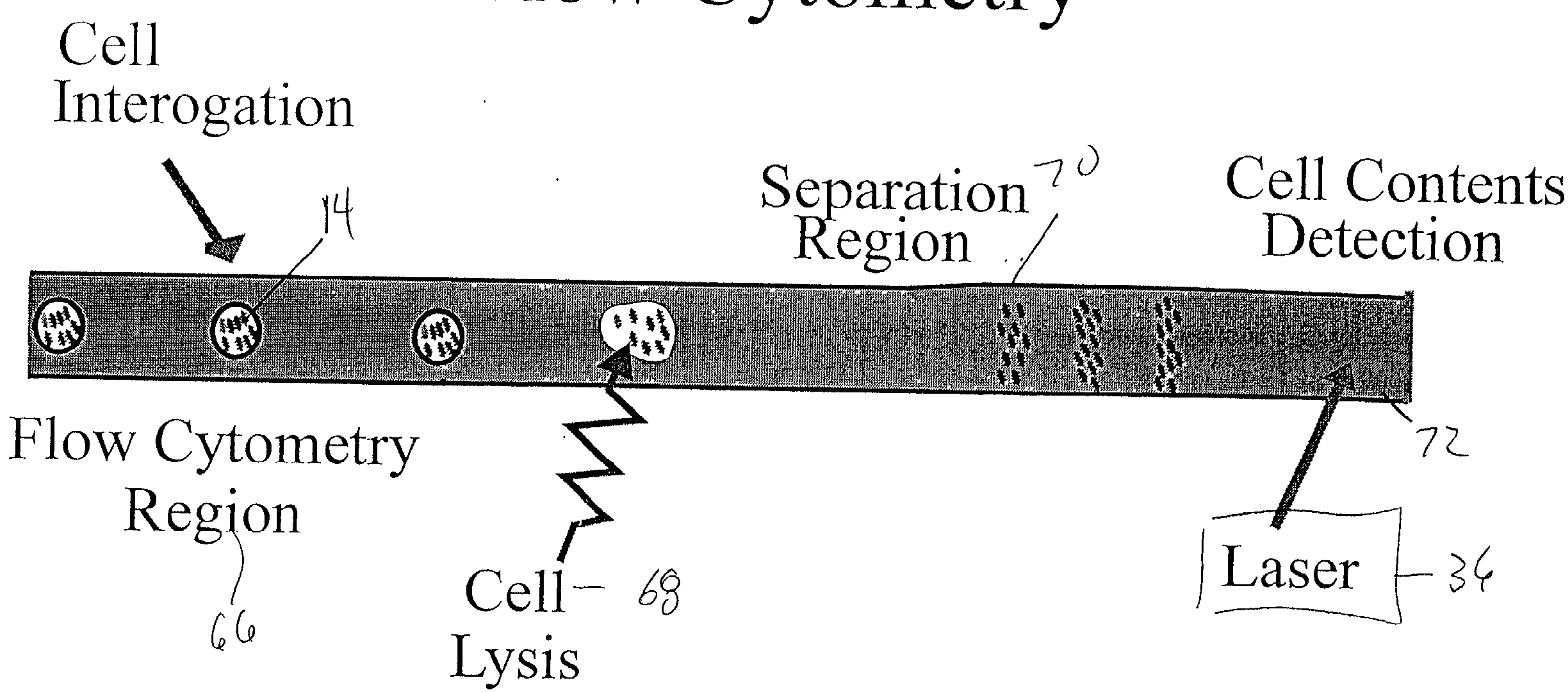
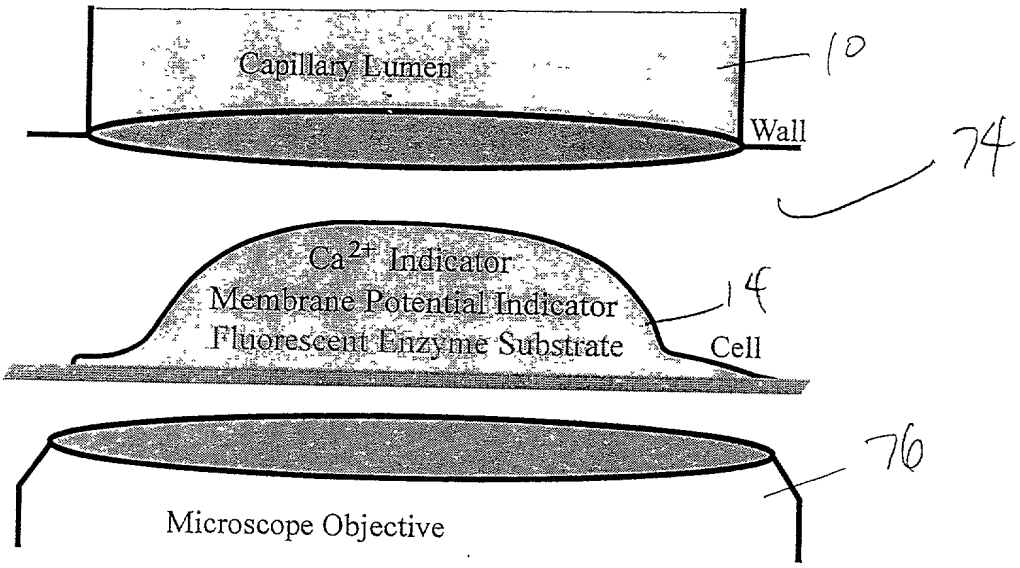


Fig. 14

Integration With Other Cellular Analysis Methods

Fluorescence Imaging



Patch Clamp

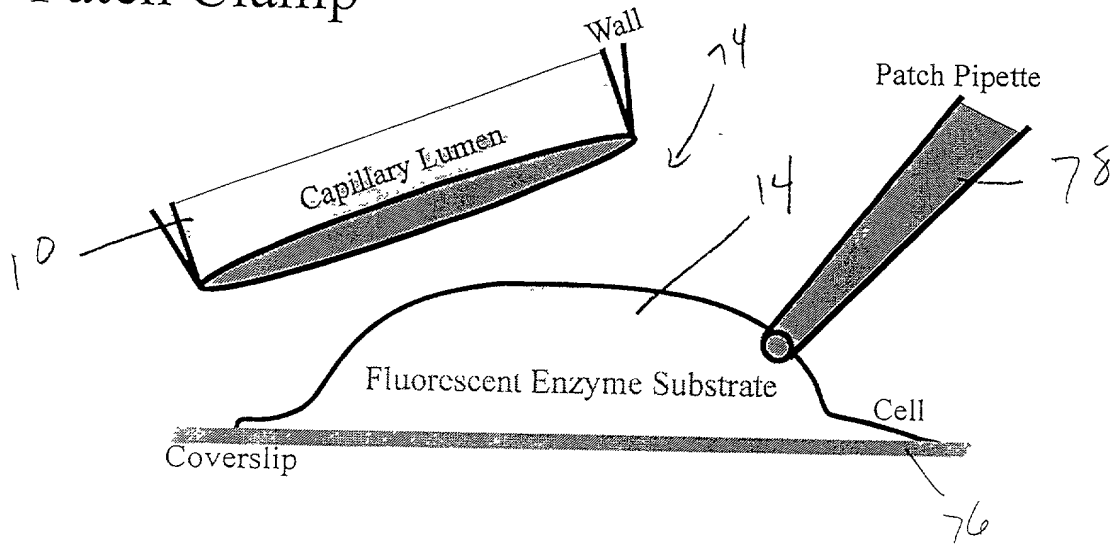


Fig. 15A

Profiling Signal Transduction Pathways in Cells with Four Reporters

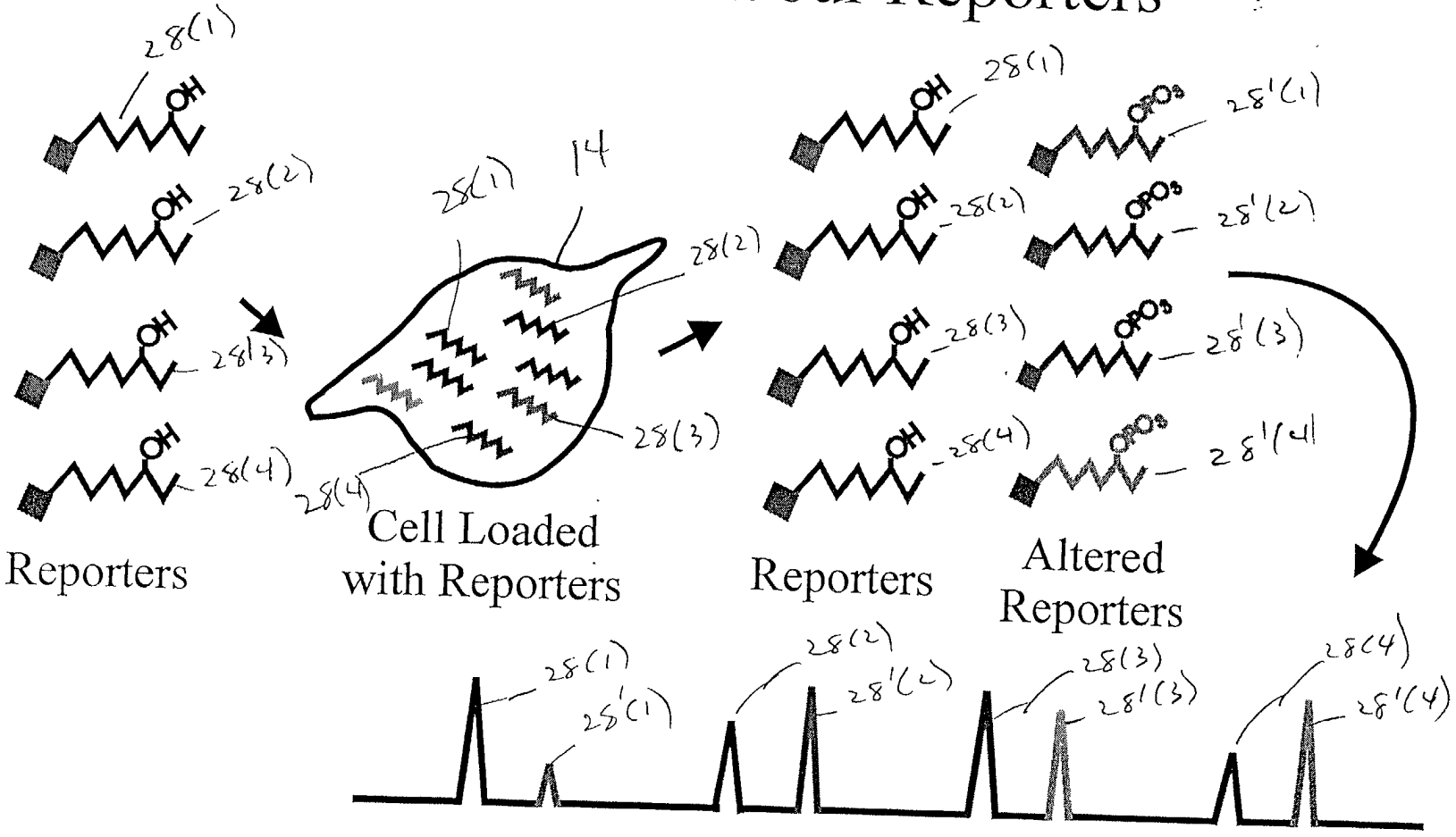


Fig. 15B

Profiling Signal Transduction Pathways in Cells with Three Reporters

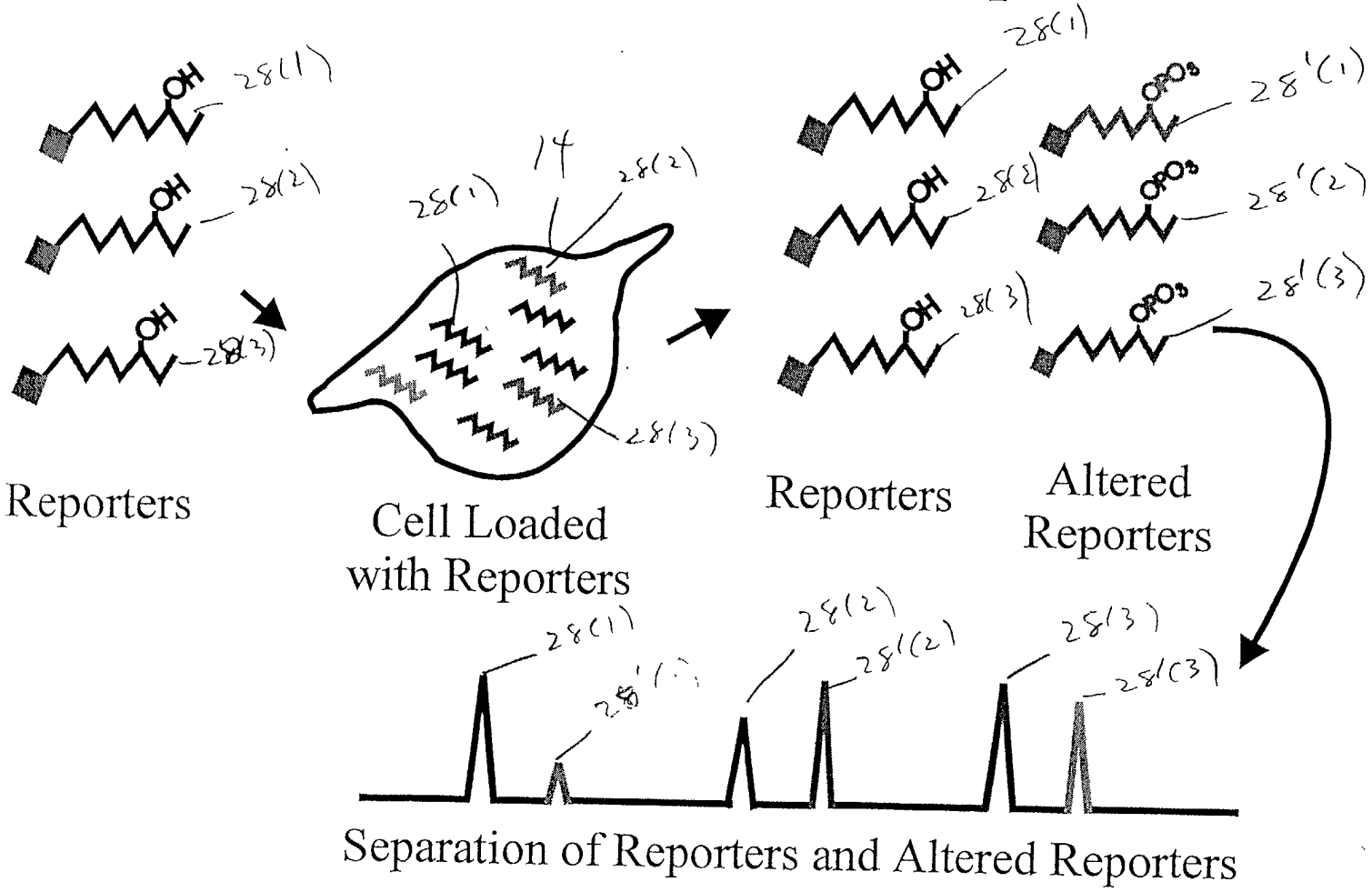


Fig. 16

Profiling Signal Transduction Pathways in Cells with Five Reporters

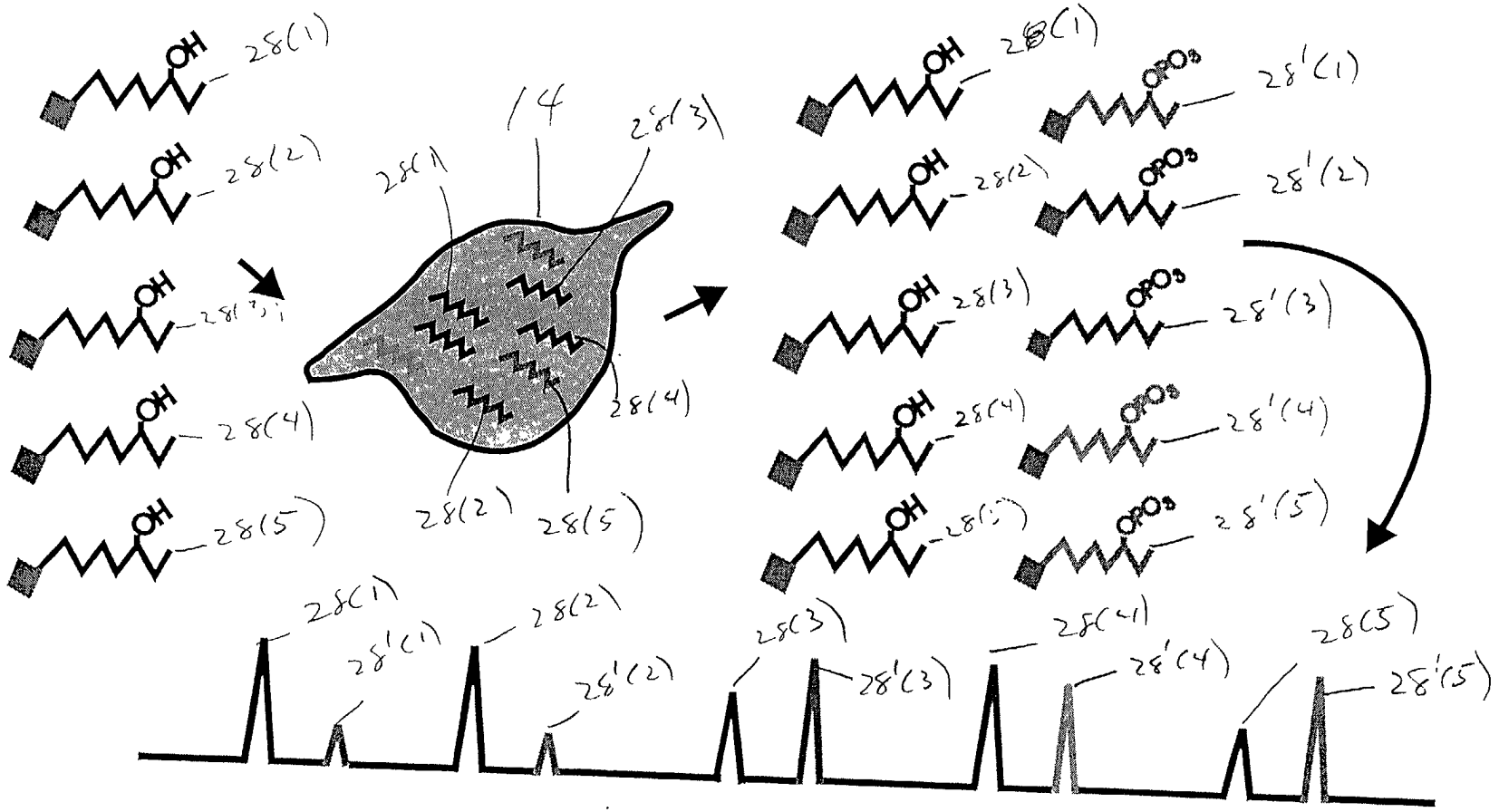


Fig. 17

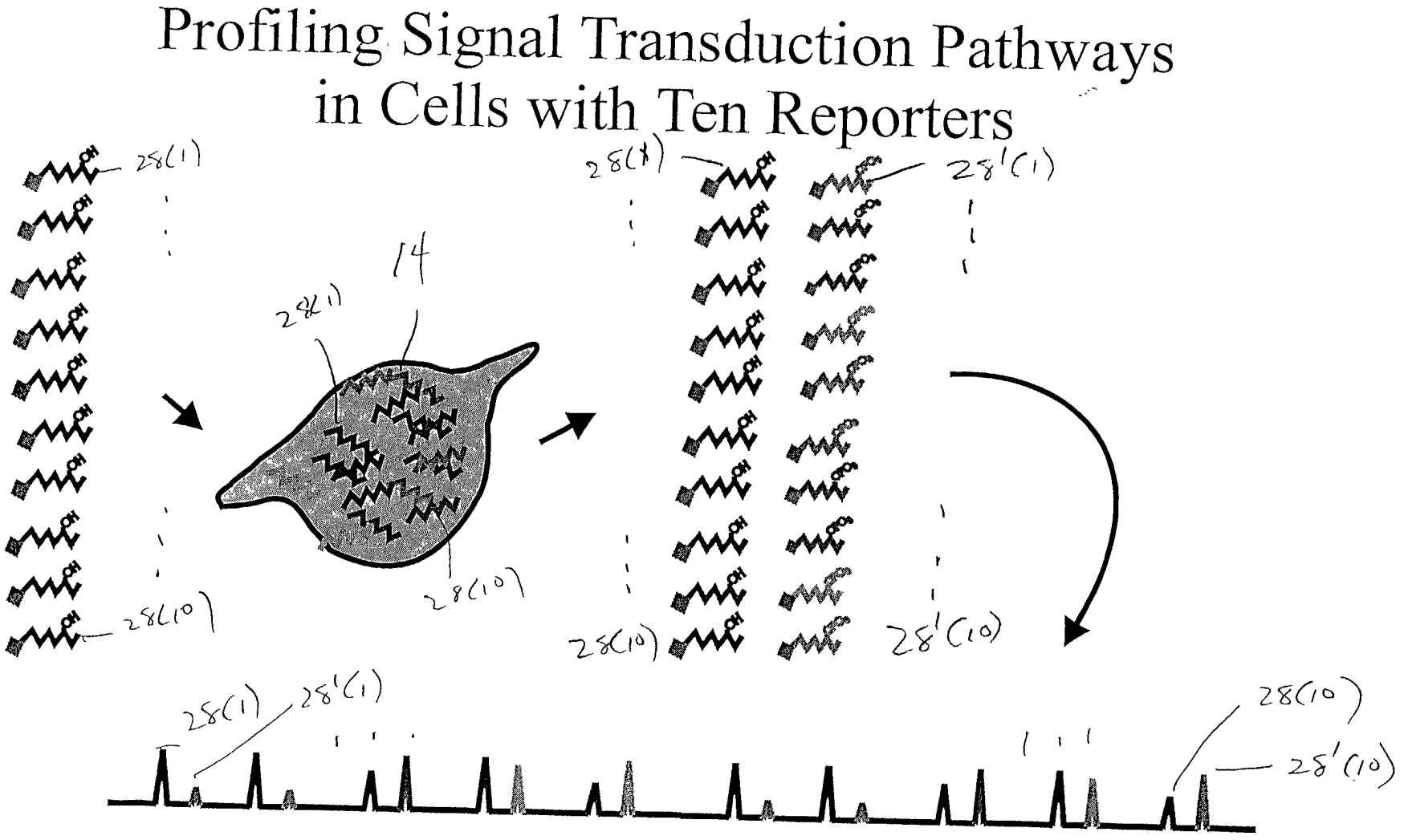

Profiling Signal Transduction Pathways
in Cells with Ten Reporters
28(1)
28(10)
14
28'(1)
28'(10)

Fig. 18

Profiling Signal Transduction Pathways in Cells with Many Reporters

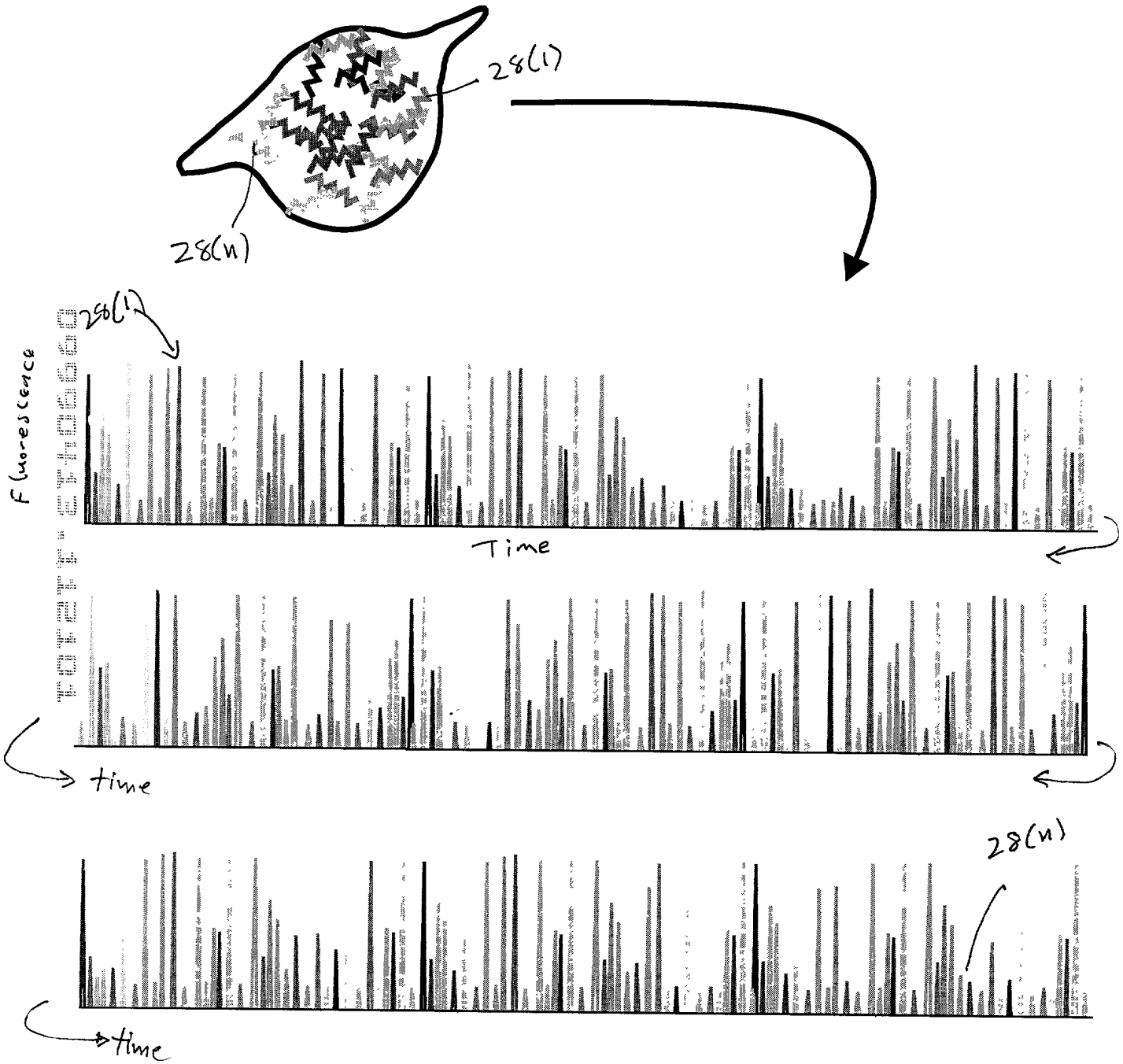


Fig. 19

Applications

- Drug Discovery and Validation

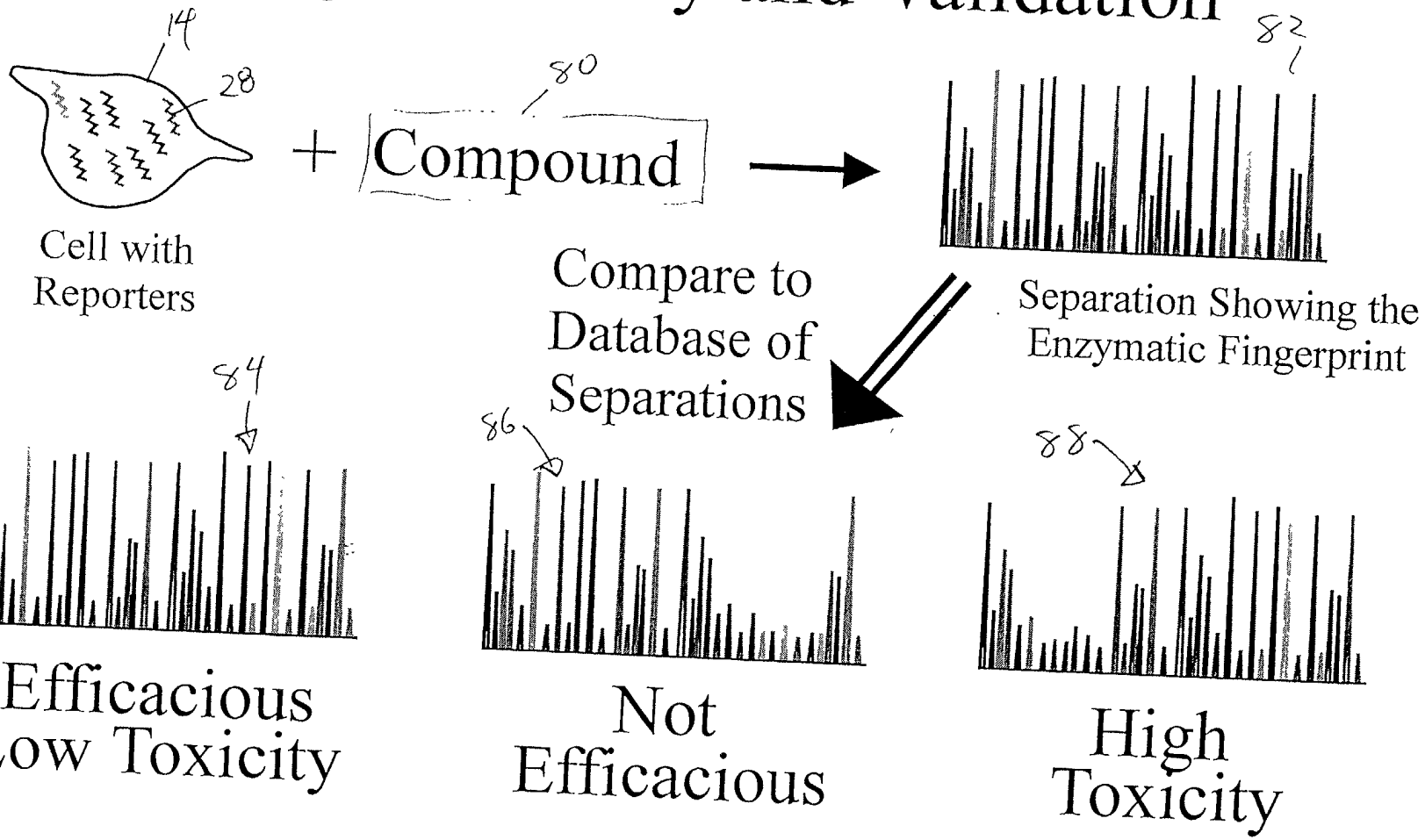


Fig. 20

Identifying the Cellular Targets of Compounds

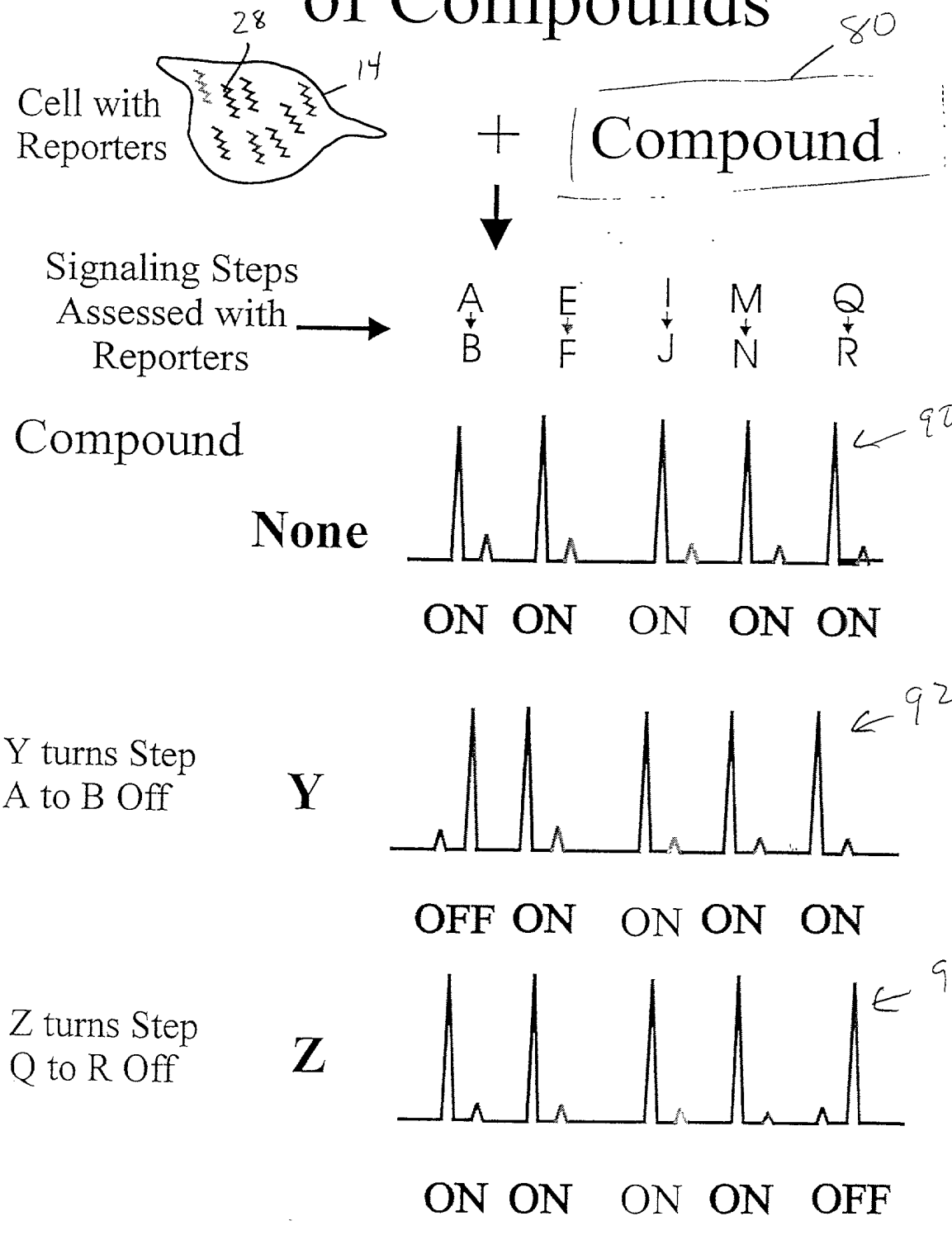


Fig. 21

Applications

- Diagnostics and Prognostics

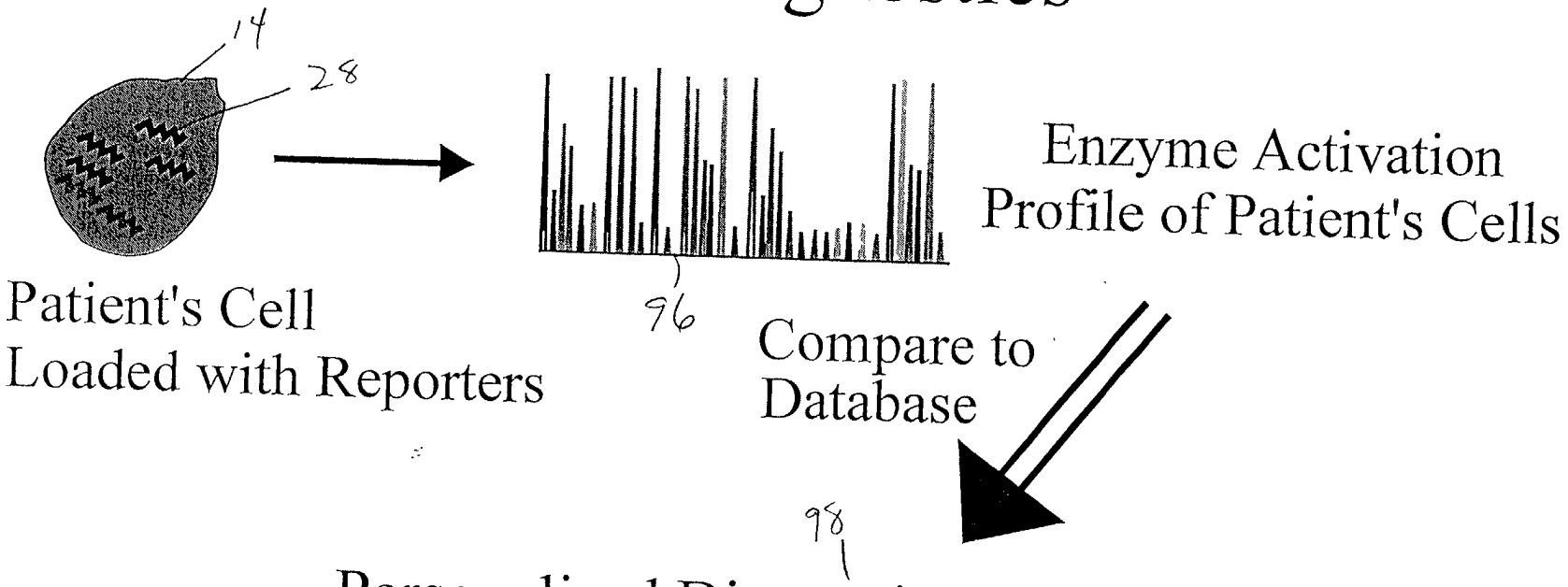


Fig. 22

Identifying and Targeting Pre-Disease or Disease States

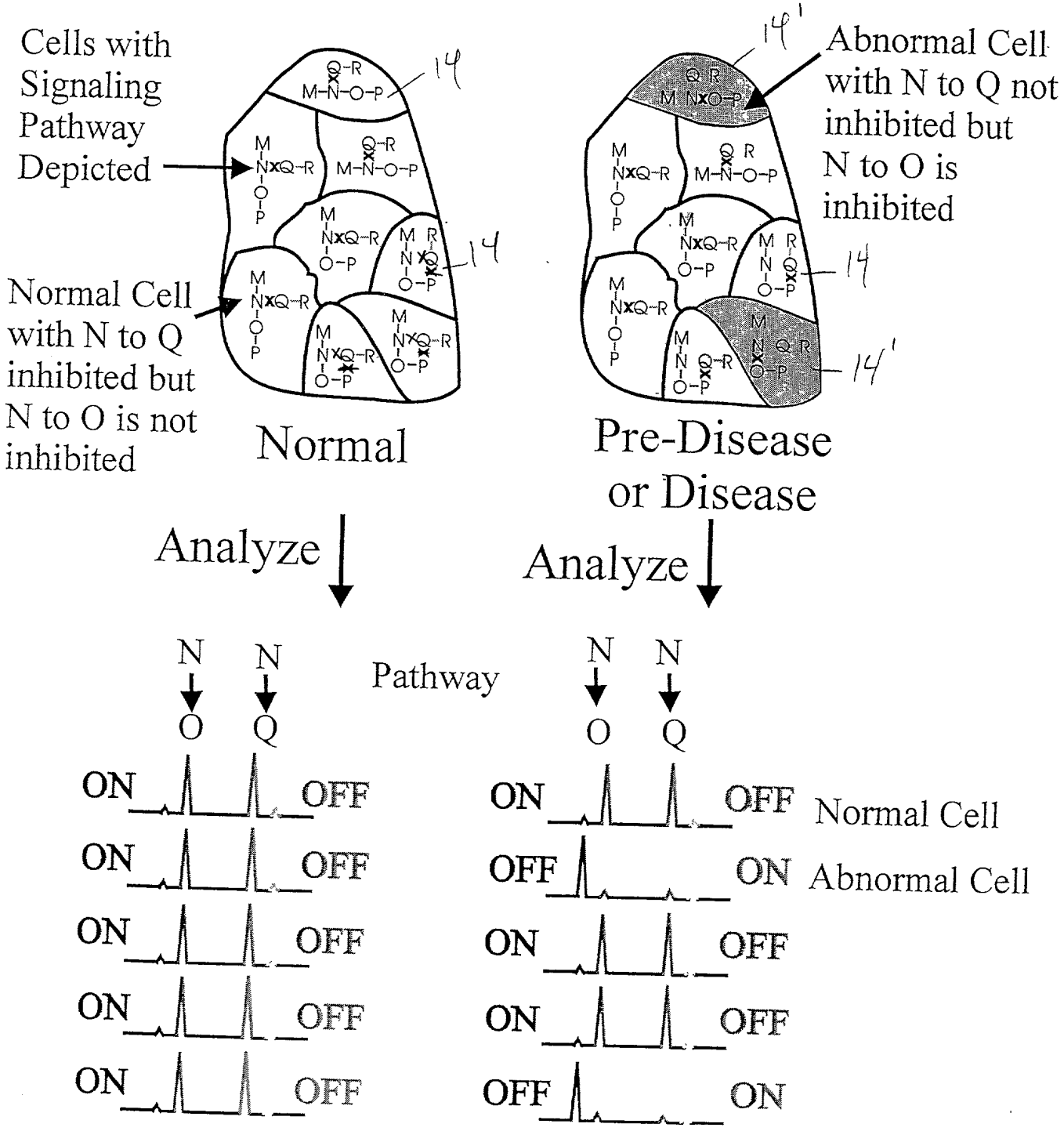
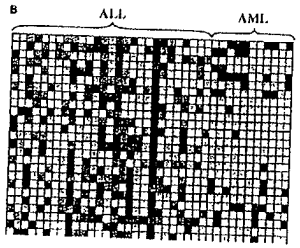


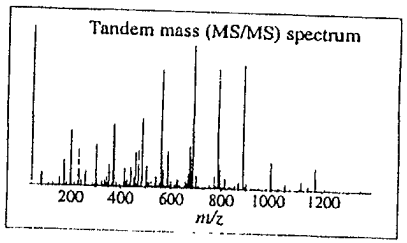
Fig. 23

Analysis of Biologic Systems



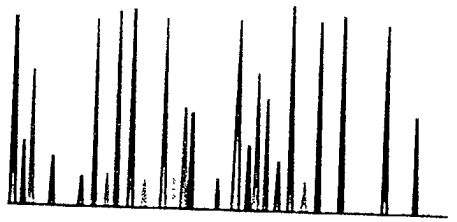
DNA Arrays

Genomics



Mass Spec.,
Protein Arrays

Proteomics



Protein Activity
Maps

Signaling

Fig. 24

Serial Analysis of Cells

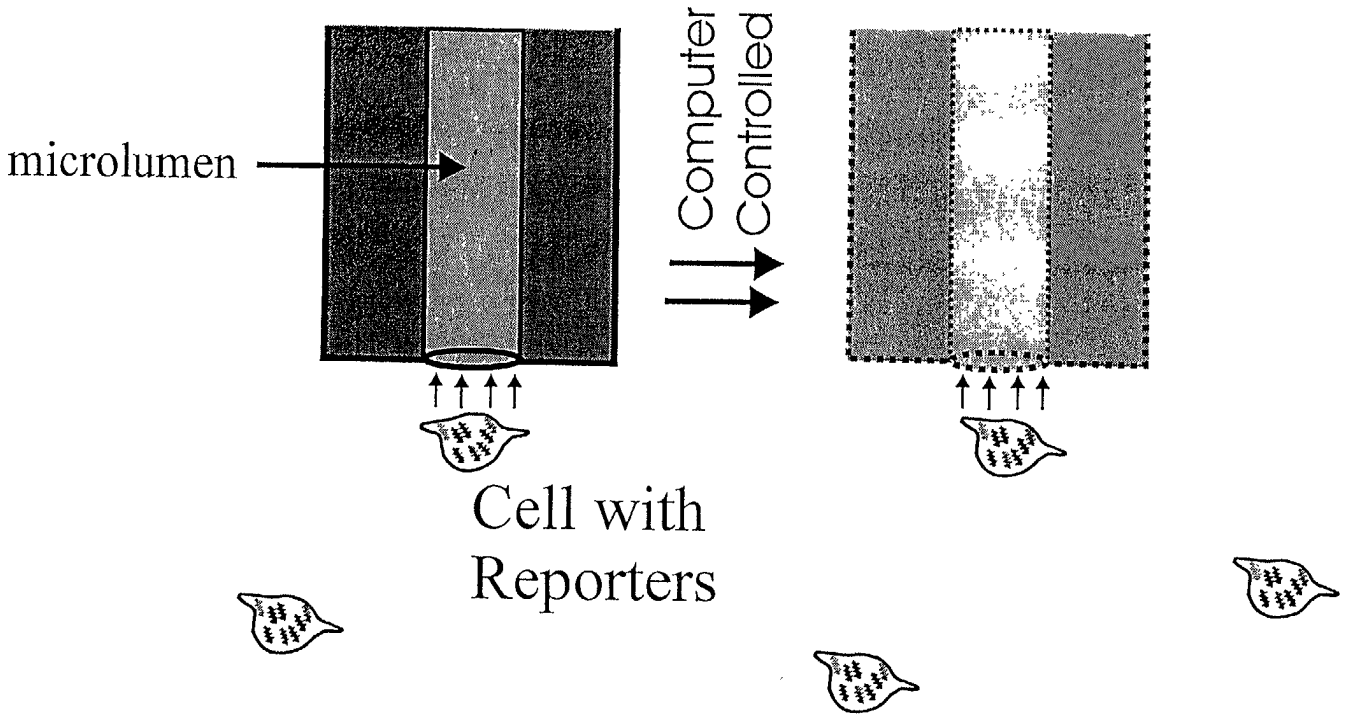
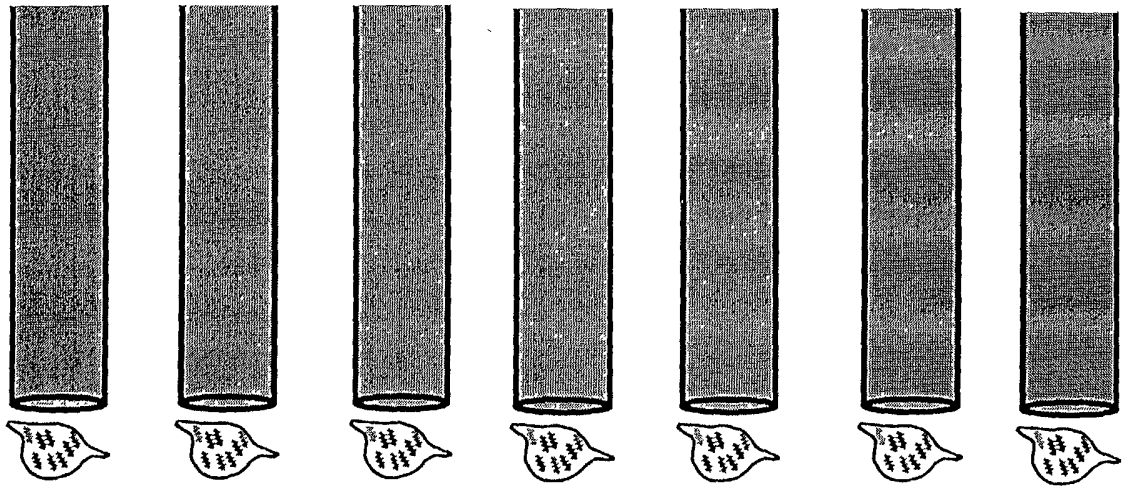


Fig. 25

Parallel Processing of Cells-

Arrays of Separation Channels



Computer-control of microlumen alignment over cells, lysis, and/or other steps.